CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being facsimile transmitted to Examiner Janet L. Epp (Group Art Unit 1635) at (703) 305-3014 of the U.S. Patent and Trademark Office on December 20, 2002.

Wanda Alleje

Wanda Alleje

Ser. No. 09/093,972
Confirmation No. 7855
Applicant: Jonathan W. NYCE

CLEAN VERSION TO SHOW REPLACEMENT CLAIMS

In the Claims

108. (Amended) An aerosolizable or sprayable composition, comprising a carrier, a nucleic acid that comprises one or more oligonuceleotide(s) (oligo(s)) effective to alleviate hyper-responsiveness to adenosine, bronchoconstriction, asthma, lung allergy] lung inflammation, or to reduce levels of adenosine receptor(s); wherein the oligo is anti-sense to an initiation codon, a coding region or a 5' or 3' intron-exon junction of a gene encoding an adenosine A_1, A_{2a}, A_{2b}, or A_3 receptor or is anti-sense to their corresponding mRNA(s), pharmaceutically and veterinarily acceptable salts of the oligo(s) or mixtures thereof.

109. (Amended) The composition of claim 108, wherein the oligo comprises up to about 10%A.

110. (Amended) The composition of claim 109, wherein the oligo comprises up to about 5%A.

111. (Amended) The composition of claim 110, wherein the oligo comprises up to about 3%A.

112. (Reiterated) The composition of claim 111, wherein the oligo is A-free.

113. (Amended) The composition of claim 108, wherein the oligo is anti-sense to the initiation codon of the mRNA, to the 5' or 3'intron-exon junctions or to sequences of the coding region comprising 2 or more G or C of the adenosine A_1 receptor gene.

114. (Amended) The composition of claim 108, wherein the oligo is anti-sense to

the initiation codon of the mRNA, to the 5' or 3'intron-exon junctions or to sequences of the coding region comprising 2 or more G or C of the adenosine A_{2a}, A_{2b} or A_3 receptors.

115. (Amended) The composition of claim 108, wherein if the oligo contains adenosine (A), at least one A is substituted by a heteroaromatic base that binds to a thymidine base but has antagonist activity or has less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, or A_3 receptors, or heteroaromatic base that has no activity or has agonist activity at the adenosine A_{2a} receptor.

116. (Amended) The composition of claim 115, wherein substantially all As are substituted by a heteroaromatic base that binds to a thymidine base but has antagonist activity or has less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} or A_3 receptors, or heteroaromatic base that has no activity or has agonist activity at the adenosine A_{2a} receptor.

117. (Amended) The composition of claim 115, wherein the heteroaromatic base is selected from a pyrimidine or purine substituted by an O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, or branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or arylcycloalkl.

118. (Amended) The composition of claim 117, wherein the pyrimidines are substituted at a 1, 2, 3, or 4 position, and the purines are substituted at a 1, 2, 3, 4, 6, 7 or 8 position.

119. (Amended) The composition of claim 118, wherein the pyrimidines or purines are one selected from theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline and xanthine.

120. (Amended) The composition of claim 116, wherein the universal base is one selected from 3 nitropyrrole-2 '-deoxynucleoside, 5-nitroindole, 2-deoxyribosyl- (5-nitroindole),

2-deoxynbofuranosyl (5 -nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3, 4-dihydropyrimido oxazine -7 -one and 2 -amino -6 -methoxyaminopurine.

121. (Amended) The composition of claim 108, wherein said nucleic acid comprises a methylated cytosine.

122. (Amended) The composition of claim 108, wherein at least one monoculeotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate,sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI), methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2 'propoxy, C-N3 18'- amine, P5 phosphoramidates, 3'-alkylamino,2 '-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-0-(2-methoxy) ethyl, 2'-0-aminopropyl, 5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone [sulfatide] (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid[s].

123. (Amended) The composition of claim 122, wherein substantially all mononucleotides are linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotrithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI), methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy,C-18 amine, N3'-P5 ' phosphoramidates, 3 '-alkylamino, 2 '-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2 '-borano, C-5 hexynyl pyrimidine, 2'-0-

aminopropyl,5-(phenylethyl) or peptide nucleic acid interbase linkages or conjugatd to a polyethylene, glycol, cholestrol, cholesteryl , dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid.

124. (Amended) The composition of claim 108, wherein the anti-sense oligo comprises 7 to 60 mononucleotides.

125. (Amended) The composition of claim 108, wherein the oligo comprises a sequence selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 and SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 and SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, phosphorotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI), methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2'-propoxy, C-18 amine, N3'-P5' phosphoramidates, 3'-alkylamino, 2'-fluoro; 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-O-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA Sulfate), dehydroepiandrosterone sulfatide (DHEA Sulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid.

126. (Amended) The composition of claim 108, wherein the nucleic acid is linked to an agent that enhances cell internalization or up-take or a cell targeting agent.

127. (Amended) The composition of claim 126, wherein the cell internalization or uptake enhancing agent is a transferrin, sialoglycoprotein or streptavidin.

128. (Reiterated) The composition of claim 126, wherein the cell targeting agent comprises a vector, and the nucleic acid is operatively linked to the vector.

129. (Reiterated) The composition of claim 128, wherein the vector comprises a prokaryotic or eukaryotic vector.

130. (Amended) The composition of claim 108, wherein the surfactant comprises a surfactant protein, phospholipid, fatty acid, or surfactant-associated protein, or mixtures thereof

SUB S

131. (Amended) The composition of claim 130, wherein the comprises a polyoxy ethylene 23 lauryl ether (Brij 35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC®), tyloxapol (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}ClO_3$ (Atovaquone®).

132. (Reiterated) The composition of claim 108, wherein the carrier comprises a biologically acceptable carrier.

134. (Reiterated) The composition of claim 108, wherein the carrier is a pharmaceutically or veterinarily acceptable carrier.

135. (Amended) The composition of claim 134, wherein the carrier is a liquid or solid carrier.

SUB S

136. (Amended) The composition of claim 108, further comprising an agent wherein said agent is a therapeutic agent, antioxidant, coloring agent, filler, volatile oil, buffering agent, dispersant, RNA inactivating agent, flavoring agent, propellant or preservative.

137. (Amended) The composition of claim 136, wherein said carrier is a pharmaceutically or veterinarily acceptable carrier.

138. (Reiterated) The composition of claim 136, wherein the RNA inactivating agent comprises an enzyme.

139. (Reiterated) The composition of claim 138, wherein the enzyme comprises a ribozyme.

140. (Reiterated) The composition of claim 108, further comprising a propellant.

141. (Reiterated) The composition of claim 108, wherein the nucleic acid is present in an amount of about 0.01 to about 99.99 w/w of the composition.

143. (Amended) The composition of claim 108, wherein said composition is a intrabuccal, intrapulmonary, respirable, nasal, inhalable, intracavitary, intraorgan, or slow release formulation.

144. (Amended) The composition of claim 143, wherein the carrier is a gaseous propellant, or solid or liquid carrier.

146. (Amended) The composition of claim 108, wherein said composition is a powder, solution, suspension or emulsion.

148. (Amended) The composition of claim 108, which is an aqueous solution, alcoholic solution aqueous suspension, alcoholic suspension, oily solution, oily suspension, oil-in-water emulsion or water-in-oil emulsion.

151. (Amended) A capsule or cartridge, comprising the composition of claim 143.

152. (Amended) The composition of claim 146, comprising a sprayable or aerosolizable solid powder.

153. (Amended) The composition of claim 108, wherein the carrier comprises a hydrophobic carrier.

158. (Amended) The composition of claim 143, which comprises an intrapulmonary, intracavitary or intraorgan liquid or solid powdered formulation of particle size about 0.5μ to about 10μ, or 10μ to 500μ.

159. (Amended) The composition of claim 143, which comprises a nasal formulation of particle size 10μ to 500μ.

161. (Amended) The composition of claim 143, in bulk, or in single or multiple unit

dose form.

162. (Amended) The composition of claim 143, which is a respirable or inhalable formulation comprising a solid powdered or liquid aerosol or spray of particle size about 0.5μ to about 10μ.

163. (Reiterated) A single cell, comprising the nucleic acid of claim 108.

164. (Amended) A diagnostic or therapeutic kit for delivery of an oligonucleotide(s) (oligo(s)) comprising, in separate containers,

the delivery device of claim 222;

a nucleic acid comprising at least one oligonucleotide (oligo), their mixtures or their pharmaceutically or veterinarily acceptable salts; and

instructions for preparation of a non-liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of the nucleic acid of particle size about 0.5 to 500μ for its use

165. (Amended) The kit of claim 164, wherein the delivery device delivers single metered doses of a solid powdered or liquid aerosol or spray inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size about 0.5μ to about 10μ or 10μ to 500μ.

166. (Amended) The kit of claim 164, wherein the device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a non-liposomal nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid of particle size about 0.5μ to about 10μ or 10μ to 500μ.

167. (Amended) The kit of claim 164, wherein the delivery device comprises a pressurized device that delivers a solid powdered or liquid aerosol or spray of particle size about 0.5μ to about 10μ or 10μ to 500μ; and the nucleic acid is provided as a non-liposomal suspension,

solution, emulsion or dry powdered aerosolizable or sprayable formulation of about 0.5μ to about 10μ or 10μ to 500μ.

Cancel Claim 168.

169. (Amended) The kit of claim 164, wherein the solvent is an organic solvent[s] or an organic solvent mixed with one or more co-solvents.

170. (Amended) The kit of claim 164, wherein the device is adapted for receiving a capsule(s) or cartridge(s), and the nucleic acid is provided as a non-liposomal inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation in a capsule(s) or cartridge(s).

171. (Amended) The kit of claim 164 further comprising, in separate containers, a propellant, a pressurized means for delivery adapted for delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the delivery device the nucleic acid as an inhalable, respirable, nasal, intracavitary, intraorgan or intrapulmonary formulation of particle size about 0.5 μ to about 10μ or 10μ to 500 μ, and then joining the device with the propellant and the pressurized means.

172. (Reiterated) The kit of claim 167, wherein the pressurized inhaler further comprises a propellant and means for delivery of the propellant, and delivers the nucleic acid as a liquid or solid powdered aerosol or spray formulation.

173. (Amended) An in vivo method of delivering a pharmaceutical composition to a target polynucleotide comprising administering to the airways of a subject an aerosol or spray non-liposomal composition of particle size about 0.5 μ to about 10 μ or 10 μ to 500 μ comprising a nucleic acid(s) that comprises at least one oligonucleotide(s) (oligo(s)).

178. (Amended) The method of claim 173, wherein the composition is administered by inhalation into the subject's respiratory system.

179. (Amended) The method of claim 173, wherein the oligo(s) is(are) anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsiveness to adenosine, increased levels of adenosine,

increased levels of an adenosine receptor, bronchoconsriction, asthma, lung allergy or lung inflammation, or is anti-sense to the corresponding mRNA, and is(are) effective to reduce hyper-responsiveness to adenosine, to reduce the amount of adenosine receptor(s), to reduce the production or availability of adenosine, or to increase the degradation of mRNA encoding the adenosine receptor.

180. (Amended) The method of claim 178, wherein the oligo(s) is(are) administered directly into the subject's lung(s), intraorgan, intracavitarily, intrabuccal or intrapulmonarily.

181. (Amended) The method of claim 173, wherein the composition comprises solid powdered or liquid particles of the nucleic acid(s) about 0.5 to about 10 μ in size.

183. (Amended) The method of claim 173, wherein the composition is administered as powdered solid or liquid nucleic acid particles 10 μ to 500 μ in size.

184. (Amended) The method of claim 173, wherein the non-liposomal composition further comprises a surfactant.

185. (Amended) The method of claim 179, wherein the hyper-responsiveness to adenosine, increased levels of adenosine , increased levels of an adenosine receptor, asthma, lung allergy or lung inflammation is associated with bronchoconstriction of lung airways.

186. (Amended) The method of claim 185, wherein the hyper-responsiveness to adenosine, increased levels of adenosine, increased levels of an adenosine receptor, bronchoconstriction, lung allergy or lung inflammation is associated with allergies, COPD, asthma, ARDS, RDS, CF or side effects of adenosine administration.

187. (Amended) The method of claim 179, wherein the hyper-responsiveness to adenosine, increased levels of adenosine, increased levels of an adenosine receptor, bronchoconstriction, asthma, lung allergy or lung inflammation is associated with inflammation or an inflammatory disease.

188. (Reiterated) The method of claim 173, wherein the composition further comprises other therapeutic agents.

189. (Amended) The method of claim 188, wherein the other therapeutic agents comprise anti-adenosine A_1, A_{2b} or A_3 receptor agents or adenosine A_{2a} receptor stimulating agents other than the nucleic acid(s).

191. (Amended) The method of claim 184, wherein the surfactant comprises a surfactant protein, non-liposomal phospholipid, fatty acid or surfactant-associated protein, or a mixture thereof.

192. (Reiterated) The method of claim 173, wherein the subject is a mammal.

193. (Amended) The method of claim 192, wherein the mammal is a human [or a non-human mammal].

195. (Amended) The method of claim 173, wherein the nucleic acid is administered in an amount of about 0.005 to about 150 mg/kg body weight.

196. (Reiterated) The method of claim 195, wherein the nucleic acid is administered in an amount of about 0.01 to about 75 mg/kg body weight.

197. (Reiterated) The method of claim 196, wherein the nucleic acid is administered in an amount of about 1 to about 50 mg/kg body weight.

198. (Amended) The method of claim 173, wherein said method is a prophylactic or therapeutic method.

200. (Amended) The method of claim 179, wherein the nucleic acid is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous bases consisting of G or C; and,

(b) obtaining a second oligo 4 to 60 nucleotides long comprising a sequence that is anti-sense to the selected fragment

201. (Amended) The method of claim 173, wherein the oligo comprises up to about 10% A.

202. (Amended) The method of claim 201, wherein the oligo comprises up to about 5%

A.

203. (Amended) The method of claim 201, wherein the oligo comprises up to about 3% A.

204. (Reiterated) The method of claim 203, wherein the oligo is A-free.

205. (Amended) The method of claim 179, wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding an adenosine A_1, A_{2b} or A_3 receptor, and the composition further comprise a surfactant.

206. (Amended) The method of claim 173, wherein if the oligo contains A, wherein at least one said A is substituted with a heteroaromatic base which binds to a thymidine base but has an antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, or A_3 receptors, or a heteroaromatic base which has no activity or has agonist activity at the adenosine A_{2a} receptor.

207. (Amended) The method of claim 206, wherein substantially all As are each substituted with a heteroaromatic base which binds to a thymidine base but has an antagonist activity or less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b}, or A_3 receptors, or a heteroaromatic base[s] which has no activity or has agonist activity at the adenosine A_{2a} receptor.

208. (Amended) The method of claim 206, wherein the heteroaromatic base is a pyrimidine or purine substituted by an O, halo, NH_2, SH, SO, SO_2, SO_3, COOH, branched fused primary secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, or arylcycloalkyl,

209. (Amended) The method of claim 208, wherein the pyrimidine is substituted at position 1, 2, 3 or 4, and the purine is substituted at position 1, 2, 3, 4, 6, 7 or 8.

210. (Amended) The method of claim 209, wherein the pyrimidine and purine is

theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine.

211. (Amended) The method of claim 206, wherein the heteroaromatic base comprises 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido oxazine-7-one or 2-amino-6-methodxyaminopurine.

212. (Amended) The method of claim 173, wherein said oligonucleotide comprises a methylated cytosine vicinal to a guanosine.

213. (Reiterated) The method of claim 173, further comprising modifying or substituting at least one mononucleotide of the anti-sense oligo(s) with methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, or combinations thereof.

214. (Amended) The method of claim 213, wherein substantially all mononucleotides are substituted or modified.

215. (Amended) The method of claim 173, the nucleic acid is operatively linked to an agent that enhances cell internalization or up-take, or a cell targeting agent.

216. (Amended) The method of claim 215, wherein the agent that enhances cell internalization or up-take is transferrin, asialoglycoprotein or streptavidin.

217. (Reiterated) The method of claim 215, wherein the cell targeting agent comprises a vector.

218. (Amended) The method of claim 217, wherein the vector comprises a prokaryotic or eukaryotic vector.

219. (Amended) The method of claim 179, wherein the nucleic acid comprises an

oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether,carbonate, 5'-N-carbamate,sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI) and methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-0-methoxyethyl,C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2' propoxy, C-18 amine, N3'-P5 phosphoramidates, 3 '-alkylamino, 2 '-fluoro pyrimidine, 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-O-(2-methoxy)ethyl, 2'-0-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid.

220. (Amended) The method of claim 191, wherein the surfactant is polyoxy ethylene 23 lauryl ether (Brij35®), t-octyl phenoxy polyethoxy ethanol (Triton X-100®), dipalmitoyl phosphatidyl choline (DPPC) and phosphatidyl glycerol (PG) (ALEC ®), (Exosurf®), phospholipids, fatty acids, surfactant-associated proteins (Survanta®) or $C_{22}H_{19}ClO_3$ (Atovaquone®).

221. (Amended) The method of claim 179, wherein the hyper-responsiveness to adenosine, increased levels of adenosine, increased levels of an adenosine receptor, bronchoconstriction, lung allergy or lung inflammation, is associated with asthma or a disease or condition associated with asthma.

222. (Amended) A diagnostic or therapeutic device adapted for delivering a non-liposomal respirable, inhalable, nasal, intrapulmonary, intraorgan, or intracavitary formulation of particle size about 0.5 μ to 500 μ, wherein the formulation comprises a nucleic acid(s) comprising at least one oligonucleotide (oligo(s)), or mixture thereof, or pharmaceutically or veterinarily acceptable salts thereof.

223. (Amended) The device of claim 222, wherein said device is adapted for delivering single metered doses of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size about 0.5μ to about 10 μ or 10 μ to 500 μ.

224. (Amended) The device of claim 222, wherein said device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and for producing a solid powdered or liquid aerosol or spray of particle size about 0.5 μ to about 10 μ or 10 μ to 500 μ and wherein the formulation is provided separately in said capsule(s) or cartridge(s) as a nasal, inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of particle size about 0.5 μ to about 10 μ or 10 μ to 500 μ.

225. (Amended) The device of claim 222, wherein said device is pressurized and delivers a solid powdered or liquid aerosol or spray formulation of particle size about 0.5 μ to about 10 μ or, or 10 μ to 500 μ; wherein the formulation comprises a suspension, solution, emulsion or dry powder aerosol or spray of the nucleic acid.

226. (Amended) The device of claim 225, further comprising, in separate containers: a propellant and means for delivering a solid powdered or liquid aerosol or spray, and instructions for loading into the device the formulation and joining the device with the propellant and the pressurized means for delivery.

227. (Amended) The device of claim 225, further comprising a propellant and means for delivering the formulation as a liquid or solid powdered aerosol or spray.

228. (Amended) The device of claim 222, wherein said device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s), and wherein the formulation is provided separately in the capsule(s) or cartridge(s).

229. (Amended) The kit of claim 164, wherein the oligo(s) is (are) anti-sense to the initiation codon, the coding region or the 5' or 3' region of a gene encoding a polypeptide wherein said polypeptide is an adenosine A_1 receptor, adenosine A_{2a} receptor, adenosine A_{2b} receptor, or adenosine A_3 receptor.

230. (Reiterated) The kit of claim 229, for diagnosis or treatment of sepsis, pulmonary vasoconstriction, lung inflammation, or lung allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), acute respiratory distress syndrome (ARDS), pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, emphysema or chronic obstructive pulmonary disease (COPD).

231. (Amended) The kit of claim 164, wherein the nucleic acid comprises an oligo of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, or SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7 to SEQ ID NO: 966, wherein at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'N carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino) (MMI), methyleneoxy (methylimino) (MOMI), terminal 1,3-propanediol, terminal dodecanol, 2'-O-methoxyethyl, C-5-propynyl pyrimidine, C-5 methyl cytidine, C-5 ethynyl pyrimidine, 2 'propoxy, C-18 amine, N3'-P5 phosphoramidates, 3 '-alkylamino, 2'-fluoro [÷] pyrimidine, 5-fluoro pyrimidine, 5-iodo pyrimidine, 5-bromo pyrimidine, 2'-borano, C-5 hexynyl pyrimidine, 2'-0-(2-methoxy)ethyl, 2'-0-aminopropyl, 5-(phenylethyl) or a peptide nucleic acid interbase linkages or conjugated to a polyethylene glycol, cholesterol, cholesteryl, dehyclroepiandlrosterone (DHEA), dehydroepiandrosterone sulfate (DHEASulfate), dehydroepiandrosterone sulfatide (DHEASulfatide), ubiquinone (CoQn), dolichol, poly L-lysine, sulfatidic acid or a fatty acid.

232. (Amended) The composition of claim 108, wherein, upon aerolization and spraying, said composition comprises particle sizes of about 0.5 μ to about 10 μ or 10 μ to 500 μ.

233. (Reiterated) The nucleic acid of claim 108, which is operatively linked to a vector.

234. (Amended) A cell comprising the nucleic acid of claim 233.

Please add the following claims:

--235. (New) The composition of claim 108, wherein the oligo(s) comprises up to about 15%

A.

236. (New) The composition of claim 130, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, and $C_{22}H_{19}ClO_3$.

237. (New) The kit of claim 164, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, and $C_{22}H_{19}ClO_3$.

238. (New) The kit of claim 164, wherein the delivery device delivers single metered doses of a solid powdered or liquid aerosol or spray buccal, nasal, intracavitary, intraorgan or intrapulmonary formulation of the nucleic acid of particle size of about 0.5 μ to 10 μ or 10 μ to 500 μ.

239. (New) The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray; and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as an inhalable, respirable, intrapulmonary, intracavitary or intraorgan formulation of the nucleic acid(s) of particle size about 0.5 μ to 10 μ or 10 μ to 500 μ.

240. (New) The kit of claim 164, wherein the delivery device is adapted for receiving and piercing or opening a capsule(s) or cartridge(s) and producing a solid powdered or liquid aerosol or spray, and the nucleic acid is provided separately in a piercable or openable capsule(s) or cartridge(s) as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of particle size of about 0.5 μ to 10 μ or 10 μ to 500 μ of the nucleic acid.

241. (New) The kit of claim 164, wherein the delivery device comprises a pressurized device that delivers a solid powdered or liquid aerosol or spray of particle size 10μ to 500μ; and the nucleic acid is provided as an aerosolizable or sprayable suspension, solution, emulsion or dry powder formulation of particle size 10μ to 500μ.

242. (New) The kit of claim 164, wherein the nucleic acid is provided as a buccal, nasal, intracavitary, intraorgan, or intrapulmonary formulation of particle size 10μ to 500μ.

243. (New) The kit of claim 171, wherein the nucleic acid is provided as an inhalable, respirable, intracavitary, intraorgan or intrapulmonary formulation of particle size about 5μ to 10μ.

244. (New) The device of claim 222, wherein said device delivers a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size about 0.5 μ to 10 μ.

245. (New) The device of claim 222, wherein said device delivers a solid powdered or liquid aerosol or spray formulation of the nucleic acid of particle size 10 μ to 500 μ.

246. (New) The device of claim 222, wherein said device delivers single metered doses

of the formulation as a solid powdered or liquid aerosol or spray of the nucleic acid of particle size 10μ to 500μ.

247. (New) The device of claim 222, wherein the oligo(s) is anti-sense to the initiation codon, the coding region or the 5' or 3 ' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to increased levels of adenosine or an adenosine receptor, bronchoconstriction, asthma, lung allergy, or lung inflammation, or is anti-sense to the corresponding mRNA, and is effective in reducing hyper-responsiveness to adenosine, the amount of an adenosine receptor, or the production or availability of adenosine, or in increasing the degradation of an adenosine receptor or mRNA thereof.

248. (New) The method of claim 190, wherein the surfactant is selected from the group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D, surfactant protein E, or active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinone, lysophosphatidylethanolamine, lysophosphatidylcholine. palmitoyl-lysophosnhatidylcholin. dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate diacylglycerol, cytidine diphosphate choline, choline, choline phosphate, lamellar bodies, omega-3 fatty acid, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene oxide block copolymers, non-ionic propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran side chains, poly (vinyl amine) with alkanoyl side chains, polyoxy ethylene ether, phenoxy polyethoxy alcohol, phosphatidyl choline ester, phosphatidyl ether, tyloxapol, a surfactant-associated protein and $C_{22}H_{19}ClO_3$.

249. (New) The method of claim 173, wherein the oligo comprises up to about 15%A.

250. (New) The method of claim 173, wherein the oligo(s) is (are) effective to alleviate hyper-responsiveness to adenosine or an adenosine receptor, reduce the level of adenosine, reduce the level of an adenosine receptor, or to alleviate bronchoconstriction, asthma, lung allergy or lung inflammation; wherein the oligo comprises up to and including about 15% adenosine, and is anti-

sense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding a protein associated with hyper-responsiveness to adenosine or an adenosine receptor, bronchoconstriction, asthma, lung allergy, or lung inflammation, or is anti-sense to the corresponding mRNA.

251. (New) The kit of claim 165, wherein the oligo(s) are effective to alleviate hyper-responsiveness to adenosine, to alleviate bronchoconstriction, asthma, lung allergy or lung inflammation, or to reduce the level of an adenosine receptor; wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsiveness to adenosine or an adenosine receptor, bronchoconstriction, asthma, lung allergy or lung inflammation, or is anti-sense to the corresponding mRNA; wherein the nucleic acid comprises one or more oligo(s).

252. (New) The kit of claim 164, wherein the oligo(s) are effective to alleviate hyper-responsiveness to increased levels of adenosine or adenosine receptors, or to alleviate bronchoconstriction, asthma, lung allergy, or lung inflammation, or to reduce levels of an adenosine receptor; wherein the oligo is anti-sense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a gene encoding a protein associated with hyper-responsiveness to increased levels of adenosine or an adenosine receptor, or bronchoconstriction, asthma, lung allergy or lung inflammation, or being anti-sense to the corresponding mRNA; wherein the nucleic acid comprises one or more oligo(s); wherein the kit is suitable for the diagnosis or treatment of a disease or condition associated with hypersensitivity to increased levels of adenosine or an adenosine receptor, or bronchoconstriction, lung allergy, lung inflammation or asthma.

253. (New) The method of claim 173, further comprising administering a surfactant.

254. (New) The method of claim 253, wherein the surfactant is administered in a prophylactically or therapeutically effective amount.

255. (New) The aerosolizable or sprayable composition according to claim 108 wherein a surfactant is operatively linked to the nucleic acid.

256. (New) The aerosolizable or sprayable composition according to claim 108

wherein the adenosine receptor comprises an adenosine A_{2a} or A_{2b} receptor and the composition does not contain a surfactant.

257. (New) The composition of claim 117, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or arylcycloalkl is substituted by an O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

258. (New) The composition of claim 208, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalhl, arylalkenyl, arylalkynyl, or arylcycloalkl is substituted by an O, halo, NH_2, primary, secondary or tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl or heteroaryl.

259. (New) The diagnostic or therapeutic kit of claim 164, further comprising an agent, wherein said agent is a therapeutic agent, diagnostic agent, anti-oxidant, filler, volatile oil, dispersant, flavoring agent, propellant, preservative, solvent, surfactant, buffering agent, RNA inactivating agent, agent that is internalized or up-taken by a cell, or coloring agent.--